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Burden of invasive cervical cancer in North Carolina

Sheri A. Denslow [a,*], Gabriel Knop [b], Christian Klaus [b], Noel T. Brewer [c,d], Chandrika Rao [b], Jennifer S. Smith [a,d,**]

[a] Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA
[b] North Carolina Central Cancer Registry, Raleigh, NC, USA
[c] Department of Health Behavior and Health Education, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA
[d] Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

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ABSTRACT

Objective. Cervical cancer causes over 4000 deaths yearly in the United States, although highly preventable through vaccination, screening, and early treatment. We aimed to determine demographic correlates for cervical cancer in North Carolina to identify target populations for interventions and to create a framework for state-level analyses.

Method. Data on all reported invasive cervical cancer cases from 1998 to 2007 were obtained from the North Carolina Central Cancer Registry. Age-adjusted incidence and mortality rates were estimated using population data from the National Center for Health Statistics.

Results. Cervical cancer incidence and mortality rates varied greatly by county and were inversely associated with county prosperity. Hispanic women had the highest incidence rate, black women the highest mortality rate, although white women accounted for most cases. Incidence rates remained fairly steady above age 35 and mortality rates steadily increased with age. A later stage at diagnosis was more common for older women and for women without private insurance.

Conclusion. Registry-based assessment illustrates the economic, racial, and age disparities associated with cervical cancer. This localized focus on demographic correlates is an important step toward eliminating this preventable disease and offers a template for cervical cancer prevention programs in other states.

Introduction

In the United States for the year 2011, an estimated 12,710 women were diagnosed with cervical cancer and an estimated 4290 women died from this disease (ACS, 2011), although it is highly preventable through vaccination, screening, and treatment of precancerous lesions.

Cervical cancer is caused by infection with carcinogenic human papillomavirus (HPV) (Scheurer et al., 2005). In a portion of HPV-infected women, cellular changes occur that lead to high-grade cervical precancer and, if untreated, invasive cervical cancer (Kisseljov et al., 2008). With the onset of the Papanicolau (Pap) screening test in the mid 1940s and, more recently, screening for high risk HPV types, most high-grade cervical precancerous lesions can be detected before progressing to cancer and death (Yang et al., 2008). As a further recent advance, prophylactic vaccines have become available and prevent the carcinogenic HPV types 16 and 18 that account for more than 70% of cervical cancer cases in the United States (Smith et al., 2007). However, an estimated one in four women in the United States have not received cervical cancer screening in the last three years (Rauscher et al., 2008) and less than a third of female adolescents have received the full three-dose series of HPV vaccine (CDC, 2010b).

To help plan preventive interventions for cervical cancer in North Carolina, we sought to assess the burden and geographical distribution of invasive cervical cancer to better understand which women are affected by cervical cancer. Understanding the socio-demographic disparities of cervical cancer allows a more informed effort to reduce or eliminate this disease. Our steps in North Carolina can also serve as a template to target cervical cancer reduction and elimination nationally, state by state.

Methods

Data collection

Data on invasive cervical cancer cases were obtained from the North Carolina Central Cancer Registry (CCR). The CCR operates under the authority

* Correspondence to: S.A. Denslow, Mission Hospital, 428 Biltmore Avenue, Asheville, NC 28801, USA. Fax: +1 828 213 5469.
** Correspondence to: J.S. Smith, University of North Carolina, CB 7435, Chapel Hill, NC 27599. Fax: +1 919 966 2089.
E-mail addresses: sheri.denslow@msj.org (S.A. Denslow), JenniferS@unc.edu (J.S. Smith).

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Table 1
Socio-demographic characteristics of women reported with invasive cervical cancer in North Carolina, 1998–2007.

		Incident cases		Mortalities[a]	
		Number (N = 3,652)	Percent	Number (N = 1,208)	Percent
Race	Black	947	25.9	392	32.6
	White	2,388	65.4	768	63.7
	Hispanic	200	5.5	18	1.5
	Other	117	3.2	26	2.2
Age	19–29	203	5.6	20	1.7
	30–39	786	21.5	118	9.8
	40–49	892	24.4	257	21.3
	50–59	689	18.9	245	20.4
	60–69	527	14.4	229	19.0
	70–98	555	15.2	335	27.8
Rurality	Rural	1,295	35.5	480	39.9
	Urban	2,305	63.1	714	59.3
	Unknown	52	1.4	10	0.8
Cervical Cancer Histological Types	Squamous	1,827	50.0		
	Adenocarcinoma	405	11.1		
	Clear cell	22	0.6		
	Other including serous carcinoma[b]	1,398	38.3		
SEER Summary Stage[c]	Local	1,996	54.7		
	Regional	1,139	31.2		
	Distant	337	9.2		
	Unknown	180	4.9		
Primary Insurance[d]	Private insurance	796	43.6		
	Government-sponsored insurance	686	37.6		
	Not insured	240	13.2		
	Unknown	103	5.6		

Produced by the NC Central Cancer Registry, 10/2010. Numbers are subject to change as files are updated.
[a] Data were not available on histological type, SEER summary stage or primary insurance for mortality cases.
[b] Less than 5 cases were classified as serous carcinoma.
[c] Surveillance, epidemiology and end results (SEER) summary stage for cancer severity (Young et al., 2001).
[d] Data restricted to 2003 to 2007.

granted by the North Carolina General Statute 130A-208; all health care providers are required to report cases to the CCR, which collects data from hospitals, physician reports, pathology laboratories, and freestanding treatment centers. The vital statistics unit of the State Center for Health Statistics (SCHS) provided data on cervical cancer deaths for the most recent 10 year period for which data have been tabulated, 1998–2007.

County of residence at time of diagnosis for incidence, and at death for mortality, were double checked and corrected by geocoding of the recorded address (1.9% and 1.3% were corrected, respectively). Eighty-eight percent of the incident cervical cancer cases and 94.2% of the study mortality cases were geocoded.

Data analysis

Population data from the National Center for Health Statistics (NCHS) were used as the denominators for estimating incidence rates and mortality rates, which are expressed per 100,000 female population for the ten-year period. Rates were age-adjusted where noted using the 2000 United States Census as the standard population reference (US Census Bureau, 2000). The direct method using eighteen 5-year age groups was used to calculate all age-adjusted rates by multiplying each age-specific rate by the number of people within that age group in the 2000 United States Census standard population, summing these products, and then dividing by the total population in the Census standard population. The updated bridged-race population estimates obtained from the NCHS were used to calculate race-specific incidence rates for 2003–2007 (NCHS, 2008). For estimating race-specific rates over time, a 3 year rolling time scale was used to smooth the trend lines.

Race and ethnicity were grouped into categories of black, Hispanic, white, or other. The term black is used to denote women who self-identified as African-American, non-Hispanic. The term white is used to denote women who self-identified as Caucasian, non-Hispanic. Insurance status was grouped into those with private insurance, those with government-sponsored insurance (Medicaid, Medicare or military coverage), and those with no insurance. Urban and rural residence designations were based on zip code using rural–urban commuting area codes version 2.0 developed by the Rural Health Research Center (Rural Health Research Center, 2005). The Tier System, designed by the North Carolina Department of Commerce, was used as a marker of county economic prosperity (NC Department of Commerce, 2010). We used Surveillance, Epidemiology and End Results (SEER) summary stage to describe cancer stage at diagnosis (Young et al., 2001).

Maps were designed using ESRI ArcMap 9.3.1. For confidentiality reasons, no data could be released that could potentially identify individual cases. Thus, all incidence data with a count of less than 5 were not presented.

Table 2
Invasive cervical cancer incidence and mortality rates per 100,000 women for North Carolina, stratified by county race/ethnicity, age, and Tier level 1998–2007.

	Incidence		Mortality	
Race/ethnicity	Cases	Rates	Cases	Rates
Black	947	10.6	394	4.5
Hispanic	200	18.3	18	2.0
White	2,388	7.3	770	2.2
	Incidence		Mortality	
Age (years)	Cases	Rates	Cases	Rates
19-39	988	8.2	138	1.1
40-49	892	13.9	257	4.0
50-65	999	13.9	367	5.1
65+	772	12.8	446	7.4
	Incidence		Mortality	
Tier[a]	Cases	Rates	Cases	Rates
Tier 1	875	9.8	303	3.1
Tier 2	1,242	8.6	445	2.9
Tier 3	1,526	7.2	460	2.2

Produced by the NC Central Cancer Registry, October 2010. Numbers are subject to change as files are updated.
[a] County Tier level as determined by the NC Department of Commerce; 3 indicates highest prosperity (2010).

Table 3
Invasive cervical cancer incidence and mortality rates per 100,000 women for North Carolina counties, 1998–2007.

County	Tier[a]	Incidence		Mortality	
		N	Rates	N	Rates
North Carolina		3,652	8.2	1,208	2.6
Alamance	2	63	8.5	18	2.3
Alexander	1	15	8.2	6	2.9
Alleghany	1	*	*	0	0.0
Anson	1	17	12.3	11	7.1
Ashe	2	6	3.2	5	2.5
Avery	2	6	6.5	3	2.3
Beaufort	1	26	10.6	4	1.5
Bertie	1	11	9.6	4	2.7
Bladen	1	19	9.9	6	2.9
Brunswick	3	30	6.6	11	2.3
Buncombe	3	77	6.4	31	2.3
Burke	1	50	10.8	14	2.7
Cabarrus	3	58	7.9	10	1.4
Caldwell	1	42	10.0	14	3.1
Camden	1	*	*	0	0.0
Carteret	3	22	6.9	8	1.9
Caswell	1	15	11.4	4	2.9
Catawba	2	62	7.9	24	3.0
Chatham	3	19	6.2	7	2.1
Cherokee	2	10	6.6	4	2.4
Chowan	1	12	15.1	6	6.5
Clay	1	*	*	2	2.4
Cleveland	1	52	9.9	19	3.2
Columbus	1	30	9.8	9	2.7
Craven	2	40	8.7	14	2.9
Cumberland	2	144	10.0	54	4.1
Currituck	2	6	5.5	4	3.4
Dare	2	18	10.1	4	2.1
Davidson	2	56	6.9	18	2.1
Davie	2	16	7.8	7	3.4
Duplin	2	33	13.1	15	5.5
Durham	3	76	6.4	22	1.9
Edgecombe	1	28	8.8	14	4.3
Forsyth	3	126	7.2	36	2.0
Franklin	2	25	9.2	4	1.5
Gaston	2	89	8.5	27	2.6
Gates	1	6	9.3	2	2.9
Graham	1	5	11.1	0	0.0
Granville	2	31	11.8	6	2.2
Greene	1	7	6.4	3	2.9
Guilford	3	168	7.2	62	2.5
Halifax	1	42	13.8	16	4.5
Harnett	2	49	10.1	18	3.7
Haywood	2	27	8.5	11	3.1
Henderson	3	32	5.5	11	1.8
Hertford	1	15	10.5	6	4.1
Hoke	2	20	12.8	5	3.3
Hyde	1	*	*	1	2.6
Iredell	3	66	9.4	22	3.0
Jackson	2	6	3.3	5	2.1
Johnston	3	64	9.4	14	2.2
Jones	1	5	8.6	0	0.0
Lee	2	21	7.9	7	2.4
Lenoir	1	42	12.9	9	2.5
Lincoln	2	43	11.9	13	3.5
McDowell	1	21	9.1	8	3.5
Macon	2	9	4.8	6	3.2
Madison	2	9	7.4	3	2.9
Martin	1	9	6.1	7	4.8
Mecklenburg	3	278	7.2	75	2.1
Mitchell	1	8	8.1	2	1.6
Montgomery	1	12	8.1	8	5.4
Moore	3	33	7.5	12	2.1
Nash	2	42	8.6	15	3.0
New Hanover	3	76	8.3	25	2.5
Northampton	1	11	7.5	2	1.6
Onslow	3	57	9.3	25	4.2
Orange	3	34	6.3	8	1.5
Pamlico	2	7	10.1	0	0.0
Pasquotank	2	14	7.8	2	0.8
Pender	3	25	10.4	8	2.9
Perquimans	2	5	7.3	2	2.0
Person	2	22	10.5	8	4.0
Pitt	2	62	9.2	26	3.8
Polk	2	7	5.5	5	2.7
Randolph	2	83	11.6	29	3.9
Richmond	1	30	12.1	7	2.9
Robeson	1	79	12.8	33	5.2
Rockingham	1	56	10.6	16	2.7
Rowan	2	57	8.2	24	3.2
Rutherford	1	32	9.3	10	2.6
Sampson	2	43	13.4	17	4.9
Scotland	1	27	14.0	13	6.8
Stanly	2	21	6.8	10	2.6
Stokes	2	22	9.1	5	2.0
Surry	1	36	9.3	12	2.9
Swain	2	*	*	2	2.2
Transylvania	2	*	*	2	0.6
Tyrrell	1	*	*	2	8.0
Union	3	50	7.0	15	2.2
Vance	1	20	8.3	7	2.7
Wake	3	235	6.7	58	1.8
Warren	1	9	7.5	5	4.1
Washington	1	7	7.9	3	3.2
Watauga	2	13	6.4	1	0.4
Wayne	1	49	8.3	9	1.4
Wilkes	1	26	7.5	9	2.3
Wilson	2	32	7.5	14	3.2
Yadkin	2	11	5.6	4	1.8
Yancey	2	6	5.3	4	4.1

N = number of cases.
Produced by the NC Central Cancer Registry, October 2010. Numbers are subject to change as files are updated. Age adjusted to the 2000 US Census Population. Incidence rates for 2003–2007 were based on the updated bridged-race population estimates obtained from the National Center for Health Statistics (2008). * Incidence counts less than 5 were not presented for confidentiality.
[a] County Tier level as determined by the NC Department of Commerce; 3 indicates highest prosperity (2010).

Results

A total of 3652 incident cases of invasive cervical cancer and 1208 associated deaths were reported between 1998 and 2007 in North Carolina (Table 1). The median age at diagnosis was 49 years (range 19 to 98 years). More than 45% of cases occurred in women aged 30–49 years, but more than half of deaths were in women over 50 years. Almost a third of deaths (28%) were in women 70 years and older. By absolute count, white women made up most incident cases and mortalities (65% and 64%, respectively). Black women made up the second largest racial demographic group at 26% of incident cases and 33% of deaths by count, while Hispanic women accounted for less than 6% of incident cases and 2% of deaths by count. Hispanic women, however, had the highest rate of cervical cancer at 18.3 cases per 100,000 women, followed by black women (10.6 cases per 100,000 women) and white women (7.3 cases per 100,000 women) (Table 2). A different pattern was found for mortality rates due to cervical cancer with black women having the highest mortality rate (4.5 deaths per 100,000 women), followed by white women (2.2 deaths per 100,000 women) and Hispanic women (2.0 deaths per 100,000 women).

Squamous carcinoma was the most common type of cervical cancer diagnosed accounting for 50% of cases (Table 1), followed by Adenocarcinoma (11%). Less than 1% of cases were clear cell. More than half of the reported cervical cancer cases had a SEER summary stage of local, being the least severe diagnosis. Close to a third of cases were diagnosed at regional stage, and less than 10% were diagnosed at distant stage, the most severe stage.

The age-adjusted incidence rate of invasive cervical cancer for North Carolina from 1998 to 2007 was 8.2 cases per 100,000 women (Table 3). The mortality rate was 2.6 cases per 100,000 women.

Incidence rates for this time period varied greatly between counties from 3.2 to 15.1 cases per 100,000 women. The range of mortality rates due to cervical cancer was 0 to 8.0 deaths per 100,000 women. Ten counties, clustered largely in the south central region, had both high incidence rates (>11 cases per 100,000 women) and mortality rates (>3 deaths per 100,000 women) of cervical cancer (Fig. 1).

The North Carolina Department of Commerce Tier designation is shown for each county (Table 3), with a higher Tier designating greater county prosperity (NC Department of Commerce, 2010). Age-adjusted incidence and mortality rates were inversely associated with county Tier number; the less prosperous counties in Tier 1 having higher incidence and mortality rates of cervical cancer (Table 2).

Fig. 2 illustrates the distribution of the age-specific North Carolina incidence and mortality rates for the 10 year period (1998–2007). The age-specific incidence rates for cervical cancer showed a bimodal pattern with rates peaking for women between 35–44 years (14.3–14.7 cases per 100,000 women) and 60–64 years (16.0 cases per 100,000 women). The highest mortality rate was among women over 84 years (10.4 deaths per 100,000 women).

When examined over time, invasive cervical cancer incidence rates for white and black women showed a slight decrease from 1995 to 2007 (from 8.0 to 7.3 and 13.1 to 9.5 cases per 100,000 women, respectively) (Fig. 3A). In contrast, incidence rates for Hispanic women varied over time without a consistent trend. Mortality rates for white and black women dropped from 1995 to 2007 (2.7 to 2.1 and 7.0 to 4.0 deaths per 100,000 women, respectively) (Fig. 3B). The mortality rate from cervical cancer for Hispanic women increased over the time period (0 to 2.0 cases per 100,000 women).

When assessing race and ethnicity in relation to cervical cancer severity at diagnosis, black women showed the highest percentage (11.4%) of distant stage cervical cancer as compared to other race/ethnicity groups (Fig. 4A). White and Hispanic women had similar proportions of cases diagnosed at the earlier, local stage (57.6% and 57.5%, respectively), with Hispanic women being diagnosed as distant stage the least often (6.0%).

With increasing age, the percentage of women diagnosed with earlier, local stage steadily decreased, dropping from 69% of women 19–39 to 42% of women 65 and older (Fig. 4B). Patients with private insurance were least often diagnosed with later stage cervical cancer (35.8% with distant and regional stage) as compared with those without private insurance (Fig. 4C). Women with no insurance and those with government-sponsored insurance showed similarly large percentages of later stage at cervical cancer diagnosis (53.4% and 52.1%, respectively). Most women 65 years of age and older (84%) reported having government-sponsored insurance. Our findings of a positive association between government-sponsored insurance and a later cancer stage at diagnosis could have been confounded by age as older women tend to be diagnosed at a later cancer stage. Therefore, we also assessed insurance status and stage at diagnosis separately for women 65 years and over. Within this age group, 35% of women with government-sponsored insurance and 18% of uninsured women were diagnosed with a local stage cancer, as compared to 50% of women with private insurance, showing that age alone does not explain the association between insurance status and stage at cancer diagnosis. No major difference in invasive cervical cancer stage at diagnosis appeared when we assessed differences by County Tier (prosperity) (Fig. 4D) or rurality (Fig. 4E).

Discussion

While rates of cervical cancer incidence and mortality in North Carolina are consistent with the national average, pockets exist within the state of extremely high incidence and mortality that could be targets for prevention programs aimed at reducing disparities. Twenty of North Carolina's 100 counties had incidence rates over 10.2 cases per 100,000 women per year, the highest rate estimated

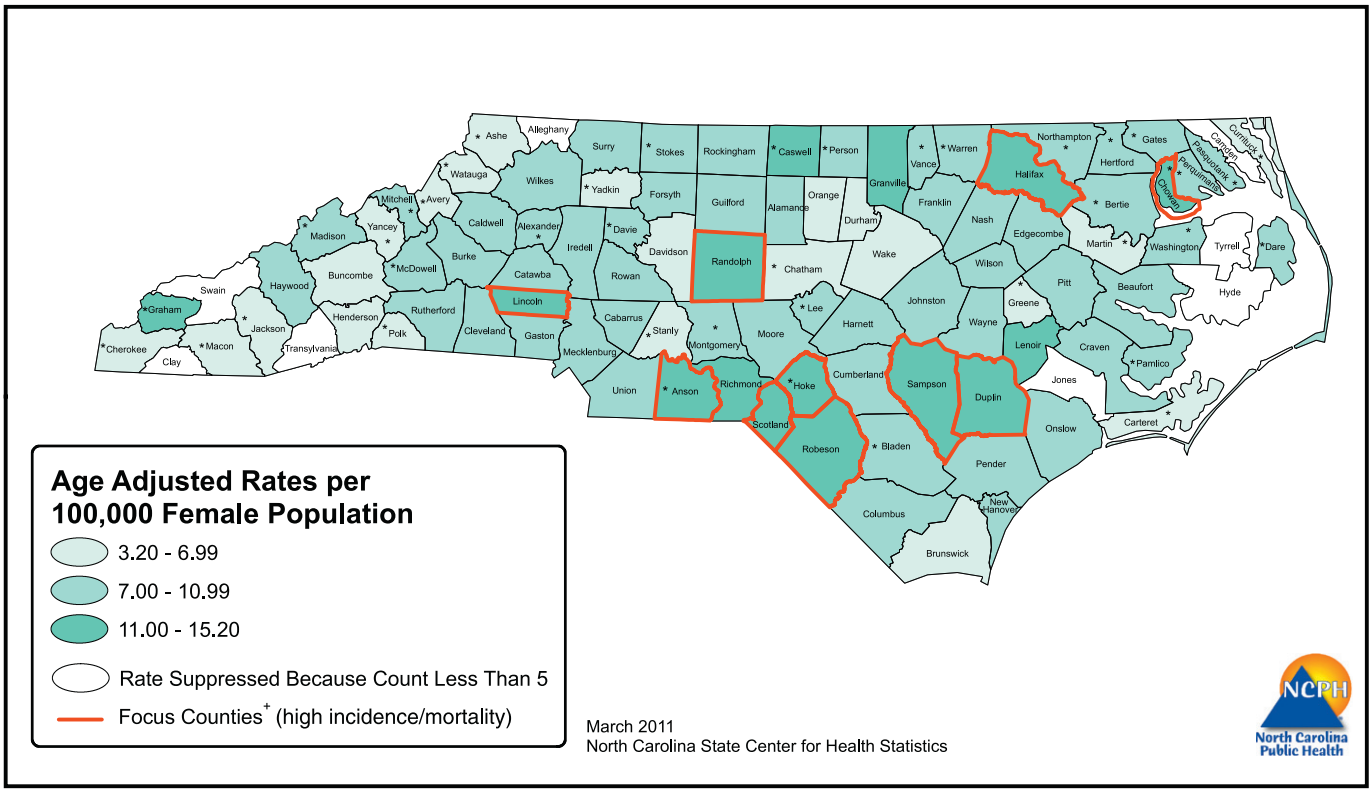

Fig. 1. North Carolina Invasive Cervical Cancer Incidence by County 1998–2007. *Rates based on less than 25 cases are unstable and should be interpreted with caution. These are indicated with an asterisk. Note: Information is subject to change as files are updated. In situ cancers are excluded. +Focus counties have a combination of a cervical cancer incidence rate greater than 11/100,000 and a cervical cancer mortality rate greater than or equal to 3/100,000.

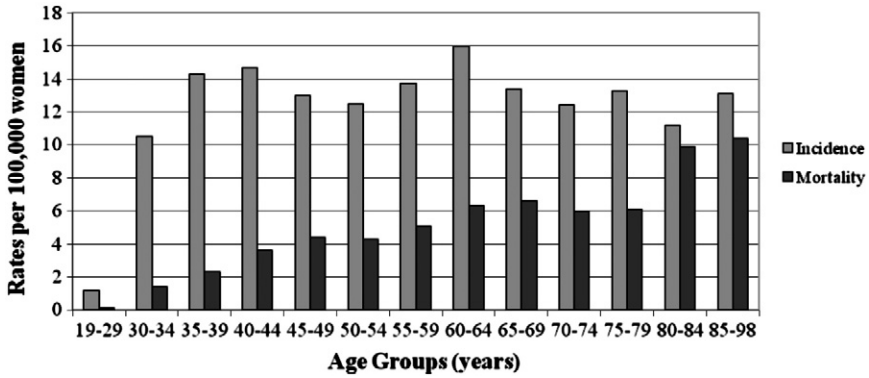

Fig. 2. Incidence and mortality rates for invasive cervical cancer per 100,000 women in North Carolina, 1998–2007. Produced by the NC Central Cancer Registry, October 2010. Numbers are subject to change as files are updated.

for any of the 50 states (Altekruse et al., 2010). Eleven counties had mortality rates above 4.2 deaths per 100,000 women per year, the highest mortality rate estimated for any of the 50 states (Altekruse et al., 2010).

The most economically distressed counties had a higher rate of both incidence and mortality of cervical cancer than the less economically distressed counties. A recent study on poverty and cancer in North Carolina found mixed results for associations of mortality from lung, breast, colon and prostate cancer with poverty (NCCHS, 2008). However, poverty in North Carolina was associated with lower rates of cancer screening and prevention behaviors (NCCHS, 2008). National data from the 2010 Behavioral Risk Factor Surveillance System (BRFSS) also show that the proportion of women who reported having a Pap test in the last three years was almost 20 percentage points lower for women

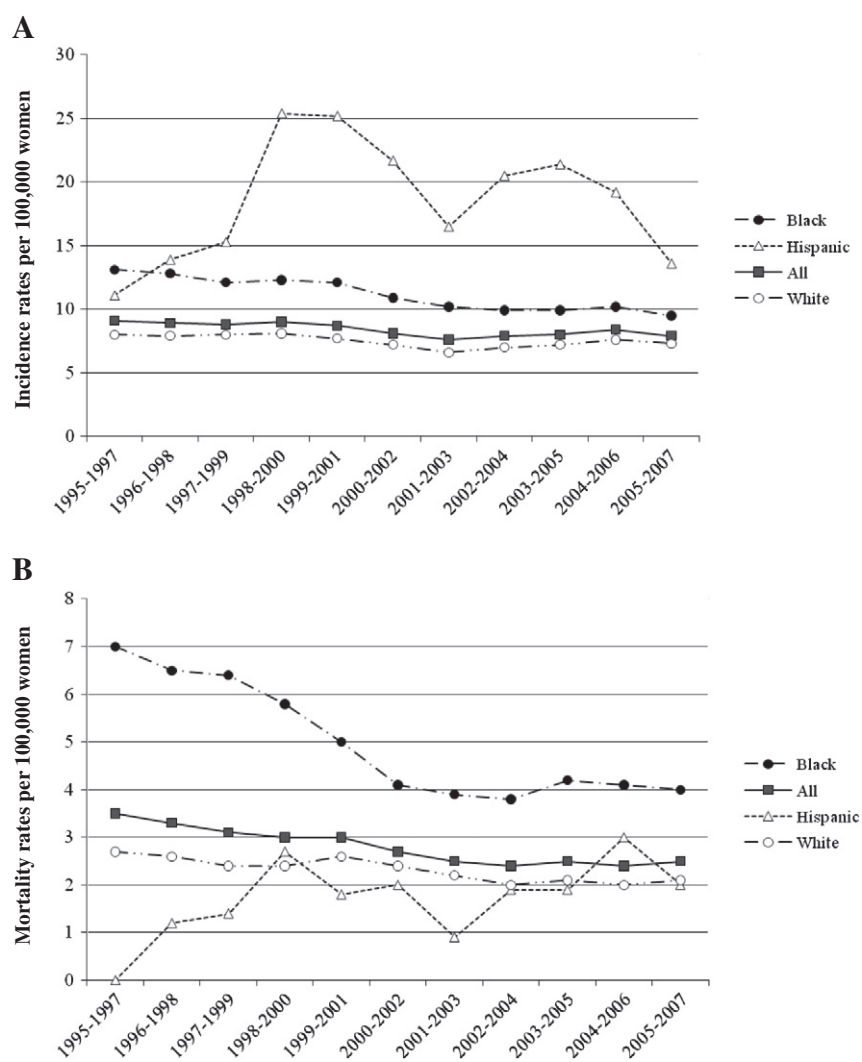

Fig. 3. Three year rolling incidence (A) and mortality (B) rates per 100,000 women over time, stratified by race and ethnicity. Produced by the NC Central Cancer Registry, October2010. Numbers are subject to change as files are updated.

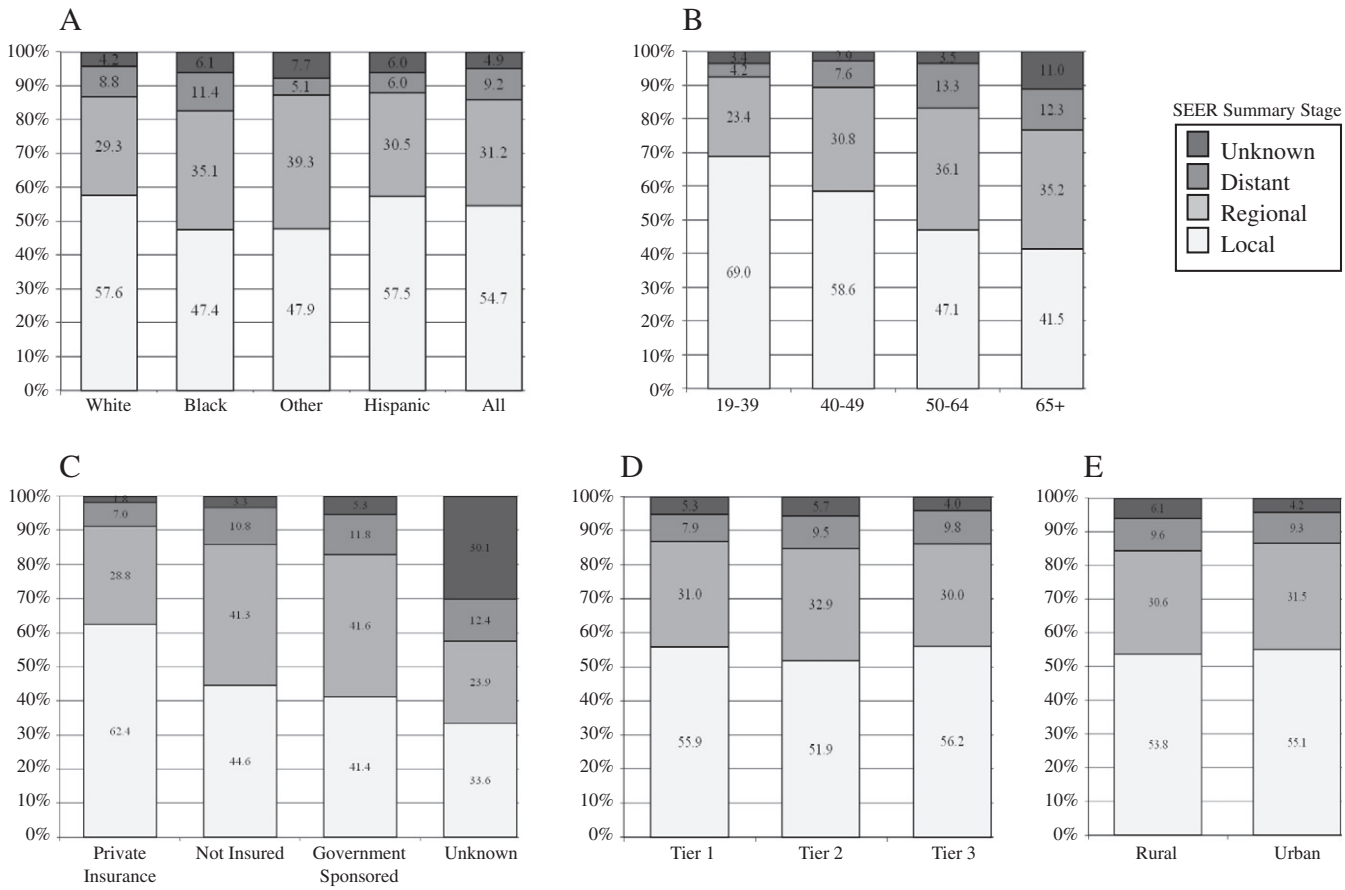

Fig. 4. SEER summary stage (Young et al., 2001) for invasive cervical cancer cases in North Carolina, 1998–2007, separated by race (A), county Tier level (NC Department of Commerce, 2010) (B), rural/urban residence (Rural Health Research Center, 2005) (C), and primary insurance type at diagnosis (D). Produced by the NC Central Cancer Registry, October 2010. Numbers are subject to change as files are updated.

with income<$15,000 as compared to women with income≥$50,000 (75% and 94%, respectively) (CDC, 2010a).

Stark differences in cervical cancer incidence and mortality rates were observed across race and ethnicity. When assessing actual numbers of cases, most cervical cancer cases in North Carolina were among white women. However, Hispanic women and black women clearly had higher incidence rates of cervical cancer as compared to white women. For mortality from cervical cancer, black women had the outlying higher rate, while Hispanic women and white women had similar, relatively lower rates of mortality. In line with mortality rates, a greater proportion of white and Hispanic women were diagnosed at an earlier, localized stage of cervical cancer than were black women. It is unclear what drives the racial disparities in cervical cancer. Nationally, black and Hispanic women are less likely than white women to have received routine Pap tests. Adjusted results from the 2000 National Health Interview Survey estimate that 73% of white women received a Pap test in the last 3 years as compared to 58% of black women and 51% of Hispanic women (Rauscher et al., 2008). North Carolina data, however, show little racial difference in self reported rates of having had a PAP test in the past 3 years (89% of black women, 84% of Hispanic women, and 83% of white women) (CDC, 2010a). Nationally, black and Hispanic women are more likely to go untreated or be undertreated for identified cervical cancer (Shavers and Brown, 2002). Race is associated with economic well-being and insurance status, factors that affect screening and prevention behaviors. In North Carolina, fewer white women (30%), aged 18–44, reported living at below the 200% income-poverty ratio, as compared to black women (57%), and Hispanic women (64%) (US Census Bureau, 2009). A similar racial trend is reported for lack of insurance with 87% of white, 75% of black, and 47% of Hispanic women, aged 18–44, reporting some form of insurance coverage (CDC, 2010a). As these socio-economic discrepancies do not fully substantiate the racial differences found for cervical cancer incidence and mortality, there must be other involved culturally-related social factors or genetic factors.

The earlier a cancer is caught, the less likely there is to be spread to surrounding systems and tissues, thus the greater chance of successful treatment (Pardo and Cendales, 2009). In addition to race (discussed previously), insurance status, and age were associated with notable differences in stage at diagnosis. For women with private insurance, most were diagnosed at an earlier, localized stage of cancer, while less than half of women with government-sponsored insurance or no insurance were diagnosed at this earlier cancer stage. There was no notable difference in stage at diagnosis for women with government-sponsored insurance and women with no insurance at all. This is possibly a sign that a proportion of uninsured women presenting at medical clinics with symptoms of late stage cervical cancer are informed of their eligibility for government-sponsored insurance at the time of diagnosis, meaning both groups of women were likely not receiving preventative care. We identified no notable difference in stage at diagnosis between women who lived in rural settings as compared to urban settings. Both groups were equally as likely to have a localized cancer. Rurality is often a factor associated with lack of access to screening due to greater distances to clinics, access to care, and other obstacles (Anderson and May, 1995; Coughlin et al., 2002). A recent national assessment, however, found no significant rural–urban disparities in stage at cancer diagnosis, though rurality was associated with increased incidence and mortality rates, suggesting the presence of other, unaccounted for influential factors (Singh, 2001).

While most cases of invasive cervical cancer occurred in women under the age of 65, the incidence rate showed relatively little variability for women between the ages of 35 and 85 and older. Additionally, women 65 and older were less likely to have an earlier, localized stage of cervical cancer at diagnosis and, correspondingly, had a higher mortality rate from cervical cancer. SEER data show that mortality rates from cervical cancer steadily increase with age nationally as well (Howlader et al., 2011). For women with adequate recent negative screening (three consecutive negative cervical cytology screens in the last decade) who are not deemed to be at high risk, the US Preventive Task Force currently recommends that screening be discontinued at age 65 and the American Cancer Society at age 70 (ACOG, 2009). Our study's observed pattern for incidence, stage at diagnosis, and mortality according to age group indicates that a non-negligible number of women 65 years and older are still acquiring cervical cancer, highlighting the fact that not all women over 65 are without risk.

This in-depth, registry-based assessment provides a clearer picture of which women in North Carolina are being diagnosed with cervical cancer and identifies gaps in our state's cervical cancer prevention health network. These cancer registry data will allow us, as a state, to better initiate targeted and appropriate interventions. A localized identification of demographic correlates for cervical cancer is an important first step in eliminating this highly preventable disease. This analysis can also serve as a model for other states as they bolster their efforts to reduce or eliminate cervical cancer in their state.

Conflict of interest statement

NB has received grants related to HPV vaccine from and/or served on advisory boards for Merck and GSK which make HPV vaccine and the CDC and FDA which set HPV vaccine policy for the US. The other authors declare that they have no conflicts of interest.

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